

fully requested, and hereby authorized, to charge Deposit Account 500438.

Rejection of claims 1-4 under §102(e)

Reconsideration of the rejection of claims 1-4 under §102(e) as being anticipated by Weiss et al. (U.S. Pat. No. 5,990,479) is respectfully requested for the following reasons. With respect to claim 4, that claim has been canceled by amendment.

1. The cited reference does not identically describe the claimed invention

As the Examiner is aware:

"Rejections under 35 USC 102 are proper only when the claimed subject matter is identically disclosed or described in the prior art... (case citations). In other words, to constitute an anticipation, all material elements recited in a claim must be found in one unit of prior art" *In re Marshall*, 198 USPQ, 344, 346 (CCPA, 1978). See also, *Acoustiflex Corp. v. Owens-Corning Fiberglass Corp.* 223 USPQ 12,13 (N.D. Illinois, 1988).

Thus, "the law requires us to determine whether the invention has been *identically* described, not whether it has been *logically* described by the reference" (*In re Arkley, Eardley and Long* 172 USPQ 524, 528).

Claim 1, and hence claims dependent thereon, has been amended to recite that the functionalized nanocrystal is comprised of a core and a shell, a capping compound comprising a compound having the formula $HS(CH_2)_nX$ wherein X is a carboxylate, and a coating comprising diaminocarboxylic acid which is operably linked to the capping compound; and that the reactive functionalities of the diaminocarboxylic acid operably link the functionalized nanocrystal to the nucleobase. Support for the amendment can be found in the specification as filed; particularly in Example 2, pages 23-26.

The Weiss et al. reference, as the Examiner correctly notes on p. 5, Point 9, of the Office Action (Paper No. 3) does not teach the functionalized nanocrystal-labeled nucleobase comprising an amino acid coating comprising diaminocarboxylic acid. A proper rejection under §102 requires that the cited

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reference identically describe or disclose the claimed invention. A comparison of the subject matter of the Weiss et al. reference with the subject matter of amended claim 1 of the present application shows that the Weiss et al. reference does not identically disclose or describe the claimed subject matter of the present invention, and thus is not a proper §102 reference.

MPEP 706.02(a). The same conclusion can be applied to new claims 23 and 26 since the Weiss et al. reference neither teaches an additional coating comprising an amino acid (claim 23) nor amino acid capping compound comprising homocysteine (claim 26) which is then coated with amino acid or a maleimide derivative (claim 26).

In view of the above considerations (e.g., the cited reference does not identically describe the claimed invention as amended), it is clear that the Weiss et al. reference is not prior art within the meaning of §102(e). Therefore, reconsideration of the rejection of claims 1-3 under §102(e) is respectfully requested.

Rejection of claims 1-5 under §103(a)

Reconsideration of the rejection of claims 1-5 under §103(a) as being obvious in view of Weiss et al. in combination with Hille et al. is respectfully requested for the following reasons. First, per the amendments herein, claim 4 has been canceled.

The basis of the Examiner's 103(a) rejections is that (a) Weiss et al. teaches the nanocrystal-labeled nucleobase of claims 1-4;

(b) Weiss et al. does not teach the at least one additional component comprising an amino acid; and

(c) Hille teach the use of a coating comprising an amino acid containing a diaminocarboxylic acid.

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1. Scope and content

The Examiner is reminded that under §103 a

"patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains...." (emphasis added).

The Applicants assert that the claimed subject matter as a whole is not obvious to one skilled in the art from the teachings of Weiss et al. in combination with Hille, as cited by the Examiner. As set forth by the Supreme Court and the Federal Circuit, the Examiner is required to determine the question of obviousness or nonobviousness by considering (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the pertinent art; and (4) secondary objective considerations. *Graham v. John Deere Co.* 383 U.S. 1, 17-18 (1966); *Orthopedic Equip. Co., Inc. v. All Orthopedic Appliances, Inc.* 707 F.2d 1376, 1379 (Fed. Cir. 1983). See also MPEP 2141.01- Scope & Content of Prior Art.

The scope and content of the references cited by the Examiner fail to teach or suggest the invention recited in amended claim 1- namely: a functionalized nanocrystal-labeled nucleobase comprising a functionalized nanocrystal operably linked to a nucleobase; wherein the functionalized nanocrystal is comprised of a core and a shell, a capping compound comprising a compound having the formula $HS(CH_2)_nX$ wherein X is a carboxylate, and a coating comprising diaminocarboxylic acid which is operably linked to the capping compound; and wherein the diaminocarboxylic acid of the functionalized nanocrystal comprises one or more reactive functionalities, and the nucleobase comprises one or more reactive functionalities, which are used to operably link the functionalized nanocrystal to the nucleobase. Hille et al.



teaches a dispersion comprising a polyurethane synthetic resin for applying to building material and furniture substrates likewood, metal, pvc and the like by spraying, flow-coating, dipping, casing, brushing, or the like which confers resistance to water, methanol, vinegar, ethanol, olive oil, cola drinks, tea, coffee, wine, beer, milk and the like (column 4, lines 50-69 onto column 5, lines 1-2). In addition to the polyurethane resin, the dispersion comprises a hydrolyzed shellac. In the process of making the polyurethane synthetic resin, a hydroxyl-containing polyester is reacted with a diisocyanate, and the resultant product is reacted with a compound which reacts with isocyanate groups ($\text{N}=\text{C}=\text{O}$) wherein such compound can comprise diamino- or dihydroxy- compounds (column 3, lines 38-68 onto column 4, lines 1-15). The Examiner is respectfully reminded that the capping compounds of the claimed functionalized nanocrystal-labeled nucleobase do not have free isocyanate groups, and that the coating taught by Hille et al., comprising the polyurethane synthetic resin and shellac, is not taught nor suggested nor expected to be useful for coating semiconductor nanocrystals. It is very clear from the scope and content of Hille et al., that the teaching of the use of a diaminocarboxylic acid is in the formation of a polyurethane synthetic resin (by binding $\text{N}=\text{C}=\text{O}$ groups)- containing dispersion for use in preserving building materials or furniture. Thus, the scope and content of the combination of cited references, when considered as a whole, fail to teach or suggest the claimed invention to one skilled in the art.

It is also respectfully pointed out that:

In deciding the question of obviousness under 35 U.S.C. §103, it is not proper to pick and choose from any one reference only so much as it will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fully suggests to one of ordinary skill in the art. *State Industries, Inc. v. A.O. Smith Corp.*, 221 USPQ 958,972 (M.D. Tenn. 1983); *In re Lunford*, 357 F.2d 380,384, 148 USPQ 716,719-720 (CCPA 1966)

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Thus, it is not proper to pick and choose a diaminocarboxylic acid component of a polyurethane synthetic resin only so that it will support a given position, to the exclusion of other parts (polyurethane resin, shellac, and use of the dispersion to coat building materials and furniture) necessary to the full appreciation of what such reference fully suggests to one of ordinary skill in the art.

One cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention (ref. to Fed. Cir.). Consequently, when prior art references require selective combination ... to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself (ref. to Fed. Cir.). Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination. *Nordberg Inc. v. Telsmith, Inc.* 881 F.Supp. 1252, 1294 (E.D.WI. 1995).

The Examiner is respectfully requested to show factual evidence that there is a teaching, suggestion or motivation found in the combination of Weiss et al. and Hille et al. for the functionalized nanocrystal-labeled nucleobase according to amended claim 1.

In order to establish a *prima facie* case of obviousness, the prior art must be sufficient to suggest making the substitution or modification necessary to achieve the claimed invention to one of ordinary skill in the art. *In re Lulu* 223 USPQ 1257, 1258 (Fed. Cir. 1984).

The Commissioner bears the burden of showing that such knowledge provided some teaching, suggestion or motivation to make the particular combination that was made by the applicant. *In re Raynes* 28 USPQ2d 1630, 1631 (Fed. Cir. 1993).

We do not think it was the intent of section 103 that either the examiner, the board or this court should substitute their own speculations for the factual knowledge of those skilled in the art. *In re Katzmahn* 146 USPQ 66,68 (CCPA 1965).

Also, the Examiner is respectfully reminded that

It is not "features" but the subject matter of the

invention "as a whole" that must be considered, 35 U.S.C. §103. That features, even distinguishing features, are "disclosed" in the prior art alone is insufficient. As above indicated, it is common to find elements or features somewhere in the prior art. Moreover, most if not all elements perform their ordained and expected function. The test is whether the claimed invention as a whole, in light of all the teachings of the references in their entireties, would have been obvious to one of ordinary skill in the art at the time the invention was made. 35 U.S.C. §103 (emphasis added). *Connell v. Sears, Roebuck & Co.* 220 USPQ 193,199 (CAFC 1983).

2. U.S. Patent No. 6,114,038

To further support the nonobviousness of the functionalized nanocrystal-labeled nucleobases according to amended claim 1, the Examiner is respectfully directed to commonly assigned U.S. Patent No. 6,114,038. The issue of the nonobviousness of the functionalized nanocrystals (including the at least one additional coating comprising a diaminocarboxylic acid), which are used to label the functionalized nanocrystal-labeled nucleobases according to amended claim 1, has been resolved by the U.S. Patent and Trademark Office. The disclosure of the functionalized nanocrystals (including the at least one additional coating comprising a diaminocarboxylic acid) was carefully reviewed by the Patent Office in the determination that these functionalized nanocrystals were novel and nonobvious. This issued patent is objective evidence of nonobviousness.

The PTO must also give weight to objective evidence of nonobviousness during patent prosecution *In re Sernaker*, 702 F.2d 989,996, 217 USPQ 1,7 (Fed. Cir. 1983).

3. Enablement

As the Examiner is aware, there is a requirement that a reference cited as prior art be enabling- See, e.g. *Azko N.V.* (citing *In re Brown* 141 USPQ 245, 249 (CCPA 1964)):

In addition, a prior art reference must be enabling, thus placing the allegedly disclosed matter in the possession of the public. *Azko N.V. v. International Trade Commission* 1 USPQ2d 1241,1245 (CAFC 1986).

See also, *In re Coker*, 175 USPQ 26 (CCPA 1972) and *In re Sheppard*, 144 USPQ 42 (CCPA 1964).

Neither the Weiss et al. reference nor the Hille et al. reference are enabling for the functionalized nanocrystal-labeled nucleobase claimed in amended claim 1. The Examiner notes that "Weiss et al. does not teach the functionalized nanocrystal-labeled nucleobase wherein the at least one additional coating comprises an amino acid containing a diaminocarboxylic acid" (Office Action, Paper No. 3, p. 5, point 9). Hille et al is enabling only for the use of a diaminocarboxylic acid (or other diamino- or dihydroxy- compound) for use in producing a polyurethane synthetic resin which is combined with shellac in forming a dispersion that can be used to coat building materials and furniture. Therefore, either reference alone, or the combination of cited references, fail as prior art because it does not place the invention recited in amended claim 1 (and dependent claims) in the possession of the public.

With the amendments and the above considerations in mind, it is the Applicants' belief that the scope and content of the combination of Weiss et al. and Hille et al. fails to make the claimed subject matter as a whole obvious within the meaning of §103. Accordingly, it is the Applicants' position that amended claim 1, and dependent claims 2 & 3, are patentable over the cited references. Therefore, it is respectfully requested that the Examiner withdraw the rejections of claims 1,2 & 3 under §103(a). Likewise, for the reasons given above, it is believed that claims 23 (reasons 1-3 above) and 26 (reasons 1 & 3 above), and their respective dependent claims, are also patentable over the combination of cited references. Support for new claims 23 and 26 can be found in the specification as filed; e.g., p. 15, lines 6-25, and p. 30, lines 3-18.

Rejection of claims 1-7 under §103(a)

Reconsideration of the rejection of claims 1-7 under

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§103(a) as being obvious in view of Weiss et al. in combination with Hille et al. and further in view of Amagi et al. is respectfully requested for the following reasons. First, per the amendments herein, claims 4 and 6 have been canceled. Amagi et al. teach an episulfide compound which is polymerized by curing to form an optical material which can be molded to the form a lens (column 14, lines 4-40). Amagi et al. teach that a mercaptocarboxylic acid is one of several compounds that can be used to cure the novel episulfide compound. Accordingly, the combination of cited references (Weiss et al., Hille et al., and Amagi et al.) fails to make the claimed invention recited in amended claim 1 obvious for the reasons as applied above to rejection under 103(a) in view of Weiss et al. and Hille et al.

1. The scope and content of the references cited by the Examiner fail to teach or suggest the invention recited in amended claim 1- namely: a functionalized nanocrystal-labeled nucleobase comprising a functionalized nanocrystal operably linked to a nucleobase; wherein the functionalized nanocrystal is comprised of a core and a shell, a capping compound comprising a compound having the formula $\text{HS}(\text{CH}_2)_n\text{X}$ wherein X is a carboxylate, and a coating comprising diaminocarboxylic acid which is operably linked to the capping compound; and wherein the diaminocarboxylic acid of the functionalized nanocrystal comprises one or more reactive functionalities, and the nucleobase comprises one or more reactive functionalities, which are used to operably link the functionalized nanocrystal to the nucleobase. The functionalized nanocrystal-labeled nucleobase suggested by Weiss et al. combined with the use of a diaminocarboxylic acid (or other diamino- or dihydroxy- compound) for use in producing a polyurethane synthetic resin which is combined with shellac in forming a dispersion that can be used to coat building materials and furniture as taught by Hille et al., in combination with the use of a mercaptocarboxylic acid to cure an episulfide compound as taught by Amagi et al. fails to make the claimed subject matter as a whole obvious within the meaning of §103.

One cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention (ref. to Fed. Cir.). Consequently, when prior art references require selective combination ... to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself (ref. to Fed. Cir.). Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination. *Nordberg Inc. v. Telsmith, Inc.* 881 F.Supp. 1252, 1294 (E.D.WI. 1995).

In order to establish a *prima facie* case of obviousness, the prior art must be sufficient to suggest making the substitution or modification necessary to achieve the claimed invention to one of ordinary skill in the art. *In re Lalu* 223 USPQ 1257, 1258 (Fed. Cir. 1984).

The Commissioner bears the burden of showing that such knowledge provided some teaching, suggestion or motivation to make the particular combination that was made by the applicant. *In re Raynes* 28 USPQ2d 1630, 1631 (Fed. Cir. 1993).

2. Additionally, U.S. Patent No. 6,114,038 is objective evidence of nonobviousness of the functionalized nanocrystals used to make the claimed functionalized nanocrystal-labeled nucleobases according to amended claim 1 (and its dependent claims).

The PTO must also give weight to objective evidence of nonobviousness during patent prosecution *In re Sernaker*, 702 F.2d 989,996, 217 USPQ 1,7 (Fed. Cir. 1983).

3. The Examiner notes that "Weiss et al. does not teach the functionalized nanocrystal-labeled nucleobase wherein the at least one additional coating comprises an amino acid containing a diaminocarboxylic acid" (Office Action, Paper No. 3, p. 5, point 9). Hille et al is enabling only for the use of a diaminocarboxylic acid (or other diamino- or dihydroxy- compound) for use in producing a polyurethane synthetic resin which is combined with shellac in forming a dispersion that can be used to coat building materials and furniture. Amagi et al. is enabling only for the use of a mercaptocarboxylic acid to cure an episulfide compound. Therefore, either reference alone, or the combination

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of cited references, fail as prior art because it does not place the invention recited in amended claim 1 (and dependent claims) in the possession of the public.

With the amendments and the above considerations in mind, it is the Applicants' belief that the scope and content of the combination of Weiss et al. and Hille et al. and Amagi et al. fails to make the claimed subject matter as a whole obvious within the meaning of §103. Accordingly, it is the Applicants' position that amended claim 1, and dependent claims 2-3, 5, and 7 are patentable over the cited references. Therefore, it is respectfully requested that the Examiner withdraw the rejections of claims 1-3, 5, and 7 under §103(a). Likewise, for the reasons given above, it is believed that claims 23 (reasons 1-3) and 26 (reasons 1 & 3), and their respective dependent claims, are also patentable over the combination of cited references.

Rejection of claims 1-7, and 10-12 under §103(a)

Reconsideration of the rejection of claims 1-7, and 10-12 under §103(a) as being obvious in view of Weiss et al. in combination with Hille et al. and further in view of Amagi et al. further in view of the Stratagene catalog (1988, p. 39) is respectfully requested for the following reasons. First, per the amendments herein, claims 4 and 6 have been canceled. Secondly, claim 10 has been amended to recite the functionalized nanocrystals recited in amended claim 1. Support for the amendment can be found in the specification as filed; particularly in Example 2, pages 23-26.

Stratagene teaches the broad concept of "gene characterization kits". Teaching of a broad concept is not a bar to patentability of novel combinations of reagents in kit form.

This broad concept does not serve as a basis for arbitrarily choosing elements from the references to attempt to fashion appellant's claimed invention. *In re Donovan and Ryan* 184 USPQ 414,420 (CCPA 1975).

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It is not "features" but the subject matter of the invention "as a whole" that must be considered, 35 U.S.C. §103. That features, even distinguishing features, are "disclosed" in the prior art alone is insufficient. As above indicated, it is common to find elements or features somewhere in the prior art. Moreover, most if not all elements perform their ordained and expected function. The test is whether the claimed invention as a whole, in light of all the teachings of the references in their entireties, would have been obvious to one of ordinary skill in the art at the time the invention was made. 35 U.S.C. §103 (emphasis added). *Connell v. Sears, Roebuck & Co.* 220 USPQ 193,199 (CAFC 1983).

Accordingly, the combination of cited references (Weiss et al., Hille et al., Amagi et al., and Stratagene) fails to make the claimed invention recited in amended claim 1 and amended claim 10 obvious for the reasons as applied above to rejection under 103(a) in view of Weiss et al., Hille et al., and Amagi et al.

1. The scope and content of the references cited by the Examiner fail to teach or suggest the invention recited in amended claim 1 (namely: a functionalized nanocrystal-labeled nucleobase comprising a functionalized nanocrystal operably linked to a nucleobase; wherein the functionalized nanocrystal is comprised of a core and a shell, a capping compound comprising a compound having the formula $\text{HS}(\text{CH}_2)_n\text{X}$ wherein X is a carboxylate, and a coating comprising diaminocarboxylic acid which is operably linked to the capping compound; and wherein the diaminocarboxylic acid of the functionalized nanocrystal comprises one or more reactive functionalities, and the nucleobase comprises one or more reactive functionalities, which are used to operably link the functionalized nanocrystal to the nucleobase); or the invention recited in amended claim 10 (namely: a kit comprising, in separate packaging: an amount of a functionalized nanocrystal having one or more reactive functionalities; and an amount of a nucleobase having one or more reactive functionalities; wherein the functionalized nanocrystal comprises a core and a shell, a capping compound comprising a compound having the formula $\text{HS}(\text{CH}_2)_n\text{X}$ wherein X is a carboxylate, and a coating comprising

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diaminocarboxylic acid which is operably linked to the capping compound). The functionalized nanocrystal-labeled nucleobase suggested by Weiss et al. combined with the use of a diaminocarboxylic acid (or other diamino- or dihydroxy- compound) for use in producing a polyurethane synthetic resin which is combined with shellac in forming a dispersion that can be used to coat building materials and furniture as taught by Hille et al., in combination with the use of a mercaptocarboxylic acid to cure an episulfide compound as taught by Amagi et al. for use in molding a lens, in combination with Stratagene's teaching of the broad concept of "gene characterization kits" fails to make the claimed subject matter as a whole obvious within the meaning of §103.

One cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention (ref. to Fed. Cir.). Consequently, when prior art references require selective combination ... to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself (ref. to Fed. Cir.). Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination. *Nordberg Inc. v. TelSmith, Inc.* 881 F.Supp. 1252, 1294 (E.D.WI. 1995).

It is wrong to use the patent... as a guide through a maize of prior art references, combining the right references in the right way so as to achieve the results of the claims in suit. Monday morning quarterbacking.... is quite improper when resolving the question of nonobviousness... *State Industries, Inc., v. A.O. Smith Corp., supra* at 973, citing *Orthopedic Equipment Co., Inc. v. United States* 212 USPQ 523.

In order to establish a *prima facie* case of obviousness, the prior art must be sufficient to suggest making the substitution or modification necessary to achieve the claimed invention to one of ordinary skill in the art. *In re Lalu* 223 USPQ 1257, 1258 (Fed. Cir. 1984).

The Commissioner bears the burden of showing that such knowledge provided some teaching, suggestion or motivation to make the particular combination that was made by the applicant. *In re Raynes* 28 USPQ2d 1630, 1631 (Fed. Cir. 1993).

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2. Additionally, commonly assigned U.S. Patent No. 6,114,038 is objective evidence of nonobviousness of the functionalized nanocrystals used to make the claimed functionalized nanocrystal-labeled nucleobases according to amended claim 1, and the functionalized nanocrystals used in the kit according to amended claim 10 (and its dependent claims).

The PTO must also give weight to objective evidence of nonobviousness during patent prosecution *In re Sernaker*, 702 F.2d 989,996, 217 USPQ 1,7 (Fed. Cir. 1983).

3. The Examiner notes that "Weiss et al. does not teach the functionalized nanocrystal-labeled nucleobase wherein the at least one additional coating comprises an amino acid containing a diaminocarboxylic acid" (Office Action, Paper No. 3, p. 5, point 9). Hille et al is enabling only for the use of a diaminocarboxylic acid (or other diamino- or dihydroxy- compound) for use in producing a polyurethane synthetic resin which is combined with shellac in forming a dispersion that can be used to coat building materials and furniture. Amagi et al. is enabling only for the use of a mercaptocarboxylic acid to cure an episulfide compound. Stratagene is enabling for only discussion of a broad concept of gene characterization kits. Therefore, either reference alone, or the combination of cited references, fail as prior art because it does not place the invention recited in amended claim 1 and amended claim 10 (and respective dependent claims) in the possession of the public.

With the amendments and the above considerations in mind, it is the Applicants' belief that the scope and content of the combination of Weiss et al. and Hille et al. and Amagi et al. and Stratagene fails to make the claimed subject matter as a whole obvious within the meaning of §103. Accordingly, it is the Applicants' position that amended claim 1, and dependent claims 2-3, 5, and 7, and amended claim 10, and dependent claims 11-12, are patentable over the cited references. Therefore, it is respectfully requested that the Examiner withdraw the rejections of claims 1-3, 5, and 7 under §103(a). Likewise, for the reasons

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given above, it is believed that claims 23 and 29 (reasons 1-3), and claims 26 and 32 (reasons 1 & 3), and their respective dependent claims, are also patentable over the combination of cited references. Support for new claims 29 and 32 can be found in the specification as filed; e.g., p. 15, lines 6-25, and p. 30, lines 3-18.

Rejection of claims 8-9 under §103(a)

Reconsideration of the rejection of claims 8-9 under §103(a) as being obvious in view of Weiss et al. in combination with Hille et al. and further in view of Amagi et al. further in view of the Stratagene catalog (1988, p. 39) is respectfully requested for the following reasons. Claim 8 has been amended to properly define the invention and to include the structural limitation (for use of functionalized nanocrystal-labeled nucleobases in a process of strand synthesis), as supported in the specification as filed (see, e.g., Example 5, pages 34-43, and particularly pages 41-43).

Terms appearing in the preamble of the claim may be deemed limitations of a claim when they give meaning to the claim and properly define the invention. *Gerber Garment Technology, Inc. v. Lectra Sys. Inc.* 916 F.2d 683,688, 16 USPQ2d 1436,1441 (Fed. Cir. 1990).

Those limitations that appear in the preamble are necessary to give meaning to the claim and properly define the invention. See, e.g., *In re Bulloch*, 604 F.2d 1362,1365, 203 USPQ 171,174 (CCPA 1979).

1. The scope and content of the combination of references cited by the Examiner fail to teach or suggest the invention recited in amended claim 8, namely: A kit for using functionalized nanocrystal-labeled nucleobases in a process selected from the group consisting of strand synthesis, sequencing a synthesized strand, and a combination thereof, the kit comprising a plurality of species of functionalized nanocrystal-labeled nucleobases, wherein an amount of each species of functionalized nanocrystal-labeled nucleobase is separately packaged, wherein each species of functionalized nanocrystal-labeled nucleobase comprises a different nucleobase type than the nucleobase type of the other species of the plurality of species of functionalized

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nanocrystal-labeled nucleobases, and wherein each species of functionalized nanocrystal-labeled nucleobase is differentially labeled with a species of functionalized nanocrystal that can emit a fluorescence emission that is spectrally resolvable as compared to the species of functionalized nanocrystals used to label the other species of the plurality of species of functionalized nanocrystal-labeled nucleobases.

As to a determination of obviousness or nonobviousness of a combination of components under §103(a), the Examiner is respectfully reminded:

That all elements of the invention may have been old (the normal situation), or some old and some new, or all new, is however simply irrelevant. Virtually all inventions are combinations and virtually all are combinations of old elements. *Environmental Designs, Ltd. v. Union Oil Co. of Cal.* 218 USPQ 865, 870 (Fed. Cir. 1983).

The combined elements must perform a new or different function, produce "unusual or surprising consequences", or cause a synergistic result (case cites). *John Zink Co. v. National Airoil Burner Co.* 613 F.2d 547 (5th Cir. 1980).

The combined elements comprising the kit according to amended claim 8 do indeed provide a new and different function. As described in detail in the specification as filed (see, e.g., p. 41 in conjunction with p. 39) a kit comprising a plurality of differentially, functionalized nanocrystal-labeled nucleobases provides a new and different function when such nucleobases are incorporated during strand synthesis; e.g., analysis of the synthesized strand allows for detection of the presence and position in detection and identification of the nucleobase (and hence the synthesized strand, such as in sequencing) by exciting the functionalized nanocrystal-labeled nucleobases, detecting and spectrally resolving the emitted fluorescence peaks, relating the fluorescence peaks to the relevant species of the plurality of differentially, functionalized nanocrystal-labeled nucleobases incorporated in the synthesized strand.

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The scope and content of the combination of cited references (Weiss et al. in combination with Hille et al. and further in view of Amagi et al. further in view of the Stratagene catalog) fail to teach, suggest, or make obvious, the novel combination of components in the kit according to amended claim 8 and its new and different function.

By statute and by case law, a combination patent is judged in terms of all of its components. *United States v. Adams* 383 U.S. 39, 86 S. Ct. 798 (1966).

More particularly, the combination of cited references is silent on a kit for use in a method of strand synthesis wherein the plurality of component functionalized nanocrystal-labeled nucleobases are differentially labeled, are incorporated therein, and are spectrally resolvable in facilitating the use. That Stratagene teaches the broad concept of "gene characterization kits". Teaching of a broad concept is not a bar to patentability of novel combinations of reagents in kit form. In fact, despite this teaching of a broad concept by Stratagene of the benefits of combining reagents into a kit form, over 220 patents have been issued since 1988 claiming kits containing nucleotides (see, Exhibit 1, attached hereto; objective evidence of non-obviousness).

The PTO must also give weight to objective evidence of nonobviousness during patent prosecution *In re Sernaker*, 702 F.2d 989,996, 217 USPQ 1,7 (Fed. Cir. 1983).

Further, the motivation exists to develop new kits as well. But again, it is the novel combination of components in the kit according to amended claim 8, and that it provides a new and different function, which makes the claimed kit nonobvious over the scope and content of the combination of cited references.

It is wrong to use the patent in suit as a guide through a maize of prior art references, combining the right references in the right way so as to achieve the results of the claims in suit. *State Industries, Inc., v. A.O. Smith Corp., supra* at 973, citing *Orthopedic Equipment Co., Inc. v. United States* 212 USPQ 523.

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Accordingly, it is the Applicants' position that amended claim 8, and dependent claim 9, are patentable over the cited references. Therefore, it is respectfully requested that the Examiner withdraw the rejection of claims 8-9 under §103(a).

In view of the above, favorable action on this application is respectfully requested. The Applicants invite and encourage Examiner Chakrabarti to call the Applicants' attorney at (614) 818-1170 ext. 201 if there are any questions concerning this communication, or if the Examiner feels there are discussions which would expedite prosecution of this application.

Respectfully submitted,
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